

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY PCT (Chapter II of the Patent Cooperation Treaty)

REC'D 27 JAN 2005

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference X-15950	<b>FOR FURTHER ACTION</b> <small>See Form PCT/IPEA/416</small>	
International application No: PCT/US2004/000019	International filing date (day/month/year) 21.01.2004	Priority date (day/month/year) 24.01.2003
International Patent Classification (IPC) or national classification and IPC C07K16/24, C12N15/13, C12N15/85, C12N5/10, A61K39/395, A61P19/02, A61P37/00, A61P25/00		
<b>Applicant</b> <b>APPLIED MOLECULAR EVOLUTION, INC et al.</b>		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> <i>(sent to the applicant and to the International Bureau) a total of sheets, as follows:</i>  <input type="checkbox"/> <i>sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</i>  <input type="checkbox"/> <i>sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</i></p> <p>b. <input type="checkbox"/> <i>(sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)), containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</i></p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>		
Date of submission of the demand 01.12.2004	Date of completion of this report 28.01.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Rankin, R Telephone No. +31 70 340-4659	



# INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/US2004/000019

## Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.  
 This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:  
 international search (under Rules 12.3 and 23.1(b))  
 publication of the international application (under Rule 12.4)  
 international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the elements\* of the international application, this report is based on (replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):

### Description, Pages

1-40 as originally filed

### Claims, Numbers

1-35 as originally filed

### Drawings, Sheets

1-31 as originally filed

a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3.  The amendments have resulted in the cancellation of:  
 the description, pages  
 the claims, Nos.  
 the drawings, sheets/figs  
 the sequence listing (specify):  
 any table(s) related to sequence listing (specify):
4.  This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).  
 the description, pages  
 the claims, Nos.  
 the drawings, sheets/figs  
 the sequence listing (specify):  
 any table(s) related to sequence listing (specify):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

the entire international application;

claims Nos. 30, 31, 34

because:

the said international application, or the said claims Nos. 30, 31, 34 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

no international search report has been established for the said claims Nos.

the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

has not been furnished

does not comply with the standard

the computer readable form

has not been furnished

does not comply with the standard

the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**International application No.  
PCT/US2004/000019**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

Novelty (N)

Yes: Claims 1-35  
No: Claims

Inventive step (IS)

Yes: Claims  
No: Claims 1-35

Industrial applicability (IA)

Yes: Claims 1-29, 32, 33, 35  
No: Claims 30, 31, 34**2. Citations and explanations (Rule 70.7):****see separate sheet****Box No. VI Certain documents cited****1. Certain published documents (Rule 70.10)**

and / or

**2. Non-written disclosures (Rule 70.9)****see separate sheet****Box No. VIII Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

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**Supplemental Box relating to Sequence Listing**

**Continuation of Box I, item 2:**

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:
  - a. type of material:
    - a sequence listing
    - table(s) related to the sequence listing
  - b. format of material:
    - in written format
    - in computer readable form
  - c. time of filing/furnishing:
    - contained in the international application as filed
    - filed together with the international application in computer readable form
    - furnished subsequently to this Authority for the purposes of search and/or examination
    - received by this Authority as an amendment on
2.  In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
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(SEPARATE SHEET)**

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**Re Item III**

**1 Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 30, 31 and 34 relate to subject matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims (Article 34(4)(a)(i) PCT)

**Re Item V**

**2 Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

2.1 Reference is made to the following document:

D1: WO 95/01997 A (GROSS MITCHELL STUART ; HURLE MARK ROBERT (US); JACKSON JEFFREY RICHARD) 19 January 1995 (1995-01-19)

**2.2 Article 33(2) PCT**

The current application is novel with regard to the prior art for the following reasons:  
D1 discloses recombinant humanized antibodies against IL-1 beta, however, the CDRs of these antibodies differ from those in claim 1 of the present application.  
D2 relates to a method of enhancing the potency of monoclonal antibodies  
D3 discloses methods of enhancing the affinity of antibodies against IL-1 beta, however, the CDRs of these antibodies differ from those in claim 1 of the present application.

**2.3 Article 33(3) PCT**

The current application does not meet the requirements of Article 33(3) PCT because the subject matter of claims 1-35 does not involve an inventive step.

2.4 D1 represents the closest prior art and discloses humanized IL-1 beta antibodies which may be used in the treatment of diseases involving inflammation (cf page 3, lines 5-19; page 12; page 21 lines 28-39; examples, claims). The CDRs from the murine antibody SK48-E28 which confer the antigen specificity are incorporated into a human IgG1 immunoglobulin after having been altered in order to have greater affinity for IL-1 beta.

2.5 The difference between claim 1 of the present application and D1 is that the CDR sequences of the antibodies are different.

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2.6 The problem to be solved may therefore be considered as providing an alternative humanized antibody against human IL-1 beta.

2.7 ~~Claim 1 of the present application solves this problem, however this solution cannot be considered as inventive since the mere provision of an alternate antibody against a known cytokine could be carried out by the skilled person using only standard techniques (Article 33(3) PCT).~~

Claims 2-35 do not contain any subject matter which could be considered inventive (Article 22(3) PCT). The application could only be deemed inventive over the prior art if the applicant could demonstrate an unexpected or surprising technical effect, which is at present not considered to be the case.

**3 Re Item VI**

**Certain documents cited**

3.1 The following document falls within the meaning of Rule 70.10 PCT. Its content is considered as relevant for the present claims. It should be mentioned that the validity of its claimed priority and that of the present application has not been checked.

Document	Published On	Priority	Filing Date
WO 03010282	06.02.2003	14.08.2001	18.07.2002

3.2 The following document falls within the meaning of Rule 70.10 PCT. Its content is considered as relevant for the present claims. It should be mentioned that the validity of its claimed priority and that of the present application has not been checked.

Document	Published On	Priority	Filing Date
WO 03073982	12.09.2003	28.02.2002	20.02.2003